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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/254,563	03/05/99	BRONSHTEIN V	UPTINC.015A

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EXAMINER	
SAUCIER,S	
ART UNIT	**PAPER NUMBER**
1651	6

DATE MAILED: 04/28/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/254,563	Bronshtein
Examiner	**Group Art Unit**
Sandra Saucier	1651

☒ Responsive to communication(s) filed on *Feb 22, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-24* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-24* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4, 5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Claims 1-24 are pending and are considered on the merits.

Information Disclosure Statement

The listing of the references on PTO 1449 is incomplete. A proper citation includes author, title, journal, volume, number, inclusive pages, (month), YEAR. The citation is missing the YEAR OF PUBLICATION of the article.

MPEP37 CFR 1.98(b) requires that each U.S. patent listed in an information disclosure statement be identified by patentee, patent number, and issue date. Each foreign patent or published foreign patent application must be identified by the country or patent office which issued the patent or published the application, an appropriate document number, and the publication date indicated on the patent or published application. Each publication must be identified by author (if any), title, relevant pages of the publication, date and place of publication. The date of publication supplied must include at least the month and year of publication, except that the year of publication (without the month) will be accepted if the applicant points out in the information disclosure statement that the year of publication is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the particular month of publication is not in issue. The place of publication refers to the name of the journal, magazine, or other publication in which the information being submitted was published.

Citations 1, 4, 5 and 7 on the IDS filed 6/7/99 are incomplete and have not been initialed.

Specification

The disclosure is objected to because of the following informalities: It lacks an abstract printed on a separate sheet of paper.

At the beginning of the specification, the following completed information should be inserted.

This application is a 371 of PCT/US__/_____, filed _____, which claims priority to U.S. Provisional application Serial No. 60/_____, filed _____. --

Claim Rejections - 35 USC § 112

INDEFINITE

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 12 recite "characterized by". This term is indefinite because it cannot be determined if these are the only characterizations of the solution or if the solution is open to further characterizations.

Claim 3 appears to repeat the first component of the cryoprotectant solution already iterated in claim 1.

Claim 4 fails to state whether the components are intended to be the penetrating or non-penetrating cryoprotectants. Claim 2 has both.

Claims 6, 15, 21 and 24 have improper Markush groups. Only one "and" should appear in a Markush phrase.

Claim 7 recites "does not substantially damage cells". However no definition of "substantial damage" is found in the specification or claims. Thus, no definite end point is seen for "substantial damage", thus the metes and bounds of the claim are unclear.

Claim 11 recites " the rehydration solution". However, claim 2 has no rehydration solution.

Claim 13 is indefinite because it cannot be understood if the rehydration solution further comprises DMSO, EG, PG or glycerol or if this is merely the permeating cryoprotectant which was used in the first steps of the process.

Claim 17 recites "stabley stored". However, no definition of stability is seen in the specification or the claims. Thus, it cannot be determined if 95% or 90% or 80% of what activity/function or physical parameter fulfills the claim.

Claim 20, "Ficoll" appears to be a trademark. Please treat it as such. Please check on the spelling, also.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States, (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-8, 10, 16, 18-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 4980277[A].

The claims are directed to a method of preserving cells or tissue by contacting the cell or tissue with a solution comprising a 1) non-permeating co-solute (amino acids or derivatives, betaine, carbohydrate such as {aldose monosaccharide, ketose monosaccharide, amino sugar, alditol, inositol, aidonic, uronic or aldaric acid}, a sugar alcohol, disaccharide or polysaccharide), 2) a permeating cryoprotectant (DMSO, ethylene glycol, propylene glycol or glycerol) and 3) a non-permeating cryoprotectant (dextran, starch, PEG, PVP, Ficoll, peptides). Some compositions used in the method are also claimed.

The references are relied upon as explained below.

US 4980277 discloses a method of cryopreserving cells comprising treating the cells with a composition of 1) betaine (1-30%), 2) glycerol and 3) egg yolk (which contains peptides).

Claims 1-7, 16, 18-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Titterington *et al.* [U].

Titterington *et al.* disclose a method of cryopreservation of mouse embryos comprising treating the embryos with a composition containing 1) sucrose (0.75M), 2) glycerol and 3) Percoll.

Claims 1-6, 9, 10, 16, 18-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Rall *et al.* [V].

Rall *et al.* disclose a method for cryopreserving embryos comprising treating the embryos with a composition comprising 1) glucose, 2) glycerol 6.5M, 3) BSA. The concentration of the components of the solution is increased stepwise (page 682).

Claims 1-6, 10, 16, 18-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5160313 [B].

US 5160313 discloses a method of cryopreserving tissue comprising contacting the tissue with a composition comprising 1) DMEM which contains glucose, 2) DMSO, 3)fetal calf serum, example 1.

Claims 1, 6, 8-10, 22-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5217860 [C].

US 5217860 disclose a method of cryopreserving tissue comprising adding a solution containing 1) formamide, 2) DMSO and increasing the concentration of the solution according to a desired profile.

Claims 1-8, 11, 12, 15, 16, 18-24 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by WO 94/13135 [IDS].

WO 94/13135 discloses a composition for cryopreserving epithelial cells comprising 1) glutamine (4mM), 2) glycerol 15%, 3) PEG 3350 (13%), example 1 and a method of cryopreservation. The rehydration solution is tissue culture medium (page 10) which may be DMEM/Ham's F12 which contains amino acids and glucose.

Claims 1-7, 9, 11-16, 18-23 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by US 5364756 [D].

US 5364756 disclose a method of preserving cells (col. 4, l. 60) by contacting the cells with a solution comprising 1)raffinose, 2) DMSO and 3) dextran (col. 13, tables). The sample is dried using the temperature program in col. 17, l. 32-46. The sample is stored and rehydrated with a solution containing 1) DMSO, 2) trehalose, 3) dextran, col. 20, table. The rehydration solution is then diluted with culture medium.

Claims 1-7, 9-24 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by US 5800978 [E].

US 5800978 discloses a cryopreservation medium comprising 0.5M glycerol, 7.5% BSA and 0.3M glucose or 5% glucose, 10% FCS, 20% Dextran40 (Table 1). A method of cryopreservation or red cells using 5% glucose (permeant), 10% sucrose (impermeant) and 20% PVP (impermeant) (buffer #8 Table 2) and other three component combinations of cryoprotectants is shown. The general principle of using a three component cryoprotectant buffer comprising a permeant (monosaccharides or polyalcohols), impermeant (disaccharide) and a high molecular weight polymer is disclosed in Example 1. 5.7 mls of cryoprotectant buffer was added to 5 mls of cells in dextrose-saline then an additional 5.7 mls of buffer was added prior to freezing. This is a one step increase in concentration of the buffer prior to freezing. During thawing, the cells were reconstituted by dilution of the freezing buffer with a reconstitution buffer comprising PVP and glucose (example 4). In table 11, red cells after dehydration are stored at 80°C for 4-6 days. In Table 10, a mixture of glycerol, glucose, lactose and HES is added to red cells prior to lyophilization.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5364756 [D] in view of US 5217860 [C] taken with US 4865871 [E] or Rall *et al.* [V] and US 5879876 [F].

The claims are directed to a method of preserving cells or tissue by contacting the cell or tissue with a solution comprising a 1) non-permeating co-solute (amino acids or derivatives, betaine, carbohydrate such as {aldose monosaccharide, ketose monosaccharide, amino sugar, alditol, inositol, aidonic, uronic or aldaric acid}, a sugar alcohol, disaccharide or polysaccharide), 2) a permeating cryoprotectant (DMSO, ethylene glycol, propylene glycol or glycerol) and 3) a non-permeating cryoprotectant (dextran, starch, PEG, PVP,

Ficoll, peptides). Dependent claims require an increase in the concentration of the cryopreservative solution or a decrease in the concentration of the rehydration solution. Some compositions used in the method are also claimed.

The primary reference of US 5364756 lacks the use of increasing concentrations of cryoprotectant prior to freezing.

US 4865871 discloses the details of the protocol used in US 5364756 (col. 11, l. 1-18).

US 5879876 discloses a general method of diluting a cryoprotectant from a thawed tissue using Plasmalyte and mannitol (ex. 2). Plasmalyte contains glucose which is a permeant.

The other references are relied upon as explained above.

The use of an increasing concentration of cryopreservatives prior to freezing in the place of the one step addition method as disclosed by US 5364756 would have been obvious when taken with US 5217860 or Rall *et al.* which disclose stepwise increases in the concentration of cryoprotectants prior to freezing in order to decrease osmotic stress in cells/tissues. The stability of the processed tissue as disclose by US 5364756 is assume to be the same as the claimed stability because the process which produces the stable product, as claimed, is essentially the same as the process disclosed in the prior art. In particular, see US 4865871 which discloses a method of sublimation and storage of biological samples after the addition of cryoprotectants. US 5364756 also discloses diluting the cryoprotectant solution after reconstitution (col. 20, table). US 5879876 discloses that gradual dilution of the cryoprotectant after thawing lessens osmotic shock of the tissue.

The method of increasing concentrations of cryoprotectants prior to freezing and decreasing concentrations of rehydration solutions during reconstitution or thawing is well known in the art. The cryoprotectant compositions as well as the rehydration compositions are also well known in the art. Neither the claimed method nor the claimed compositions are allowed.

One of skill in the art would have been motivated at the time of invention to make this substitution in order to obtain the results as suggested by the

references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651. The supervisor for 1651 is M. Wityshyn, (703) 308-4743.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (703) 308-1084. Status inquiries must be directed to the Service Desk at (703) 308-0196. The number of the Fax Center for the faxing of papers is (703) 308-4227.

Sandra Saucier
Primary Examiner
Art Unit 1651
April 26, 2000